TITLE: A preparation of pyrimidine derivatives, useful as ghrelin receptor modulators

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PATENT ASSIGNEE(S): USA

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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005070712	A1	20050331	US 2003-671723	20030926 <--
WO 2005030734	A1	20050407	WO 2004-US31115	20040923 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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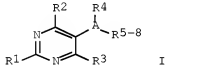
PRIORITY APPLN. INFO.: US 2003-671723 A 20030926 <--

OTHER SOURCE(S): CASREACT 142:336390; MARPAT 142:336390

GI



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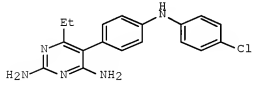

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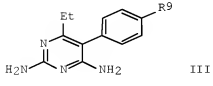


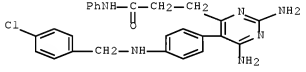
III

AB The invention relates to a preparation of pyrimidine derivs. of formula I [wherein: R1 is H, (cyclo)alkyl, aryl, CN, or haloalkyl, etc.; R2 is H, alkyl,

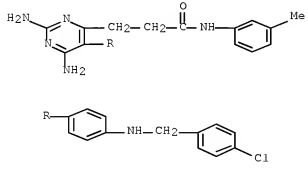
alkoxy, aryl, halogen, or haloalkyl, etc.; R3 is alkenyl, alkenyloxy, alkynyloxy, heteroarylthio, or arylthio, etc.; R4 is alkenyl, alkenyloxy, alkoxyalkyl, alkyl, or alkylthio, etc.; R5, R6, R7, and R8 are independently selected from H, alkenyl, alkyl, cyanoalkyl, alkylcarbonyl, or alkoxysulfonyl, etc.; A is (hetero)aryl, cycloalkyl, cycloalkenyl, or heterocycle], useful as ghrelin receptor modulators. The invention compds. are useful in the prevention or treatment of disorders regulated by ghrelin receptor (anorexia, cancer cachexia, eating disorders, obesity, and diabetes mellitus, etc.). For instance, pyrimidine derivative II was prepared via heterocyclization of 2-(4-nitrophenyl)-3-oxopentanenitrile with CH2N2, reduction of the obtained (nitrophenyl)pyrimidine derivative III (R9 = NO2), and subsequent reductive amination of 4-chlorobenzaldehyde by the obtained (aminophenyl)pyrimidine derivative III (R9 = NH2) (yields: heterocyclization - 27%, reduction - 90%, reductive amination - 29%). The preferred compds. stimulate ghrelin receptor with EC50 in a range of about 0.001 μM to about 0.1 μM. Other preferred compds. inhibit the activity of ghrelin receptor with IC50 in a range of about 0.001 μM to about 0.1 μM.

IT 848666-32-0P 848666-42-2P 848666-43-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrimidine derivs. useful as ghrelin receptor modulators)

RN 848666-32-0 ZCAPLUS
CN 4-Pyrimidinepropanamide, 2,6-diamino-5-[4-[[(4-chlorophenyl)methyl]amino]phenyl]-N-phenyl- (CA INDEX NAME)



RN 848666-42-2 ZCAPLUS
CN 4-Pyrimidinepropanamide, 2,6-diamino-5-[4-[[(4-chlorophenyl)methyl]amino]phenyl]-N-(3-methylphenyl)- (CA INDEX NAME)

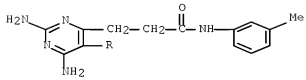


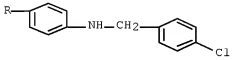
RN 848666-43-3 ZCAPLUS
CN 4-Pyrimidinepropanamide, 2,6-diamino-5-[4-[[(4-chlorophenyl)methyl]amino]phenyl]-N-(3-methylphenyl)-,

mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 848666-42-2
CMF C27 H27 Cl N6 O





CM 2

CRN 76-05-1
CMF C2 H F3 O2

IT 848666-33-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of pyrimidine derivs. useful as ghrelin receptor modulators)
RN 848666-33-1 ZCAPLUS
CN 4-Pyrimidinepropanamide, 2,6-diamino-5-(4-nitrophenyl)-N-phenyl- (CA INDEX NAME)